

Proceeding Paper

# Reuse of a Recovered, Spent Hydroprocessing Catalyst in Indole Acylations Using Cyclic Anhydrides <sup>†</sup>

Noe Martínez-Romero <sup>1,2</sup>, Eder Y. Nolasco-Terrón <sup>1,2</sup>, Mario Valle-Sánchez <sup>1,2</sup>, Marco A. García-Eleno <sup>1,2</sup>, M. V. Basavanag Unnamatla <sup>1,2</sup>, Carlos E. Barrera-Díaz <sup>1,2</sup> and Erick Cuevas-Yañez <sup>1,3,\*</sup>

<sup>1</sup> Centro Conjunto de Investigación en Química Sustentable UAEM-UNAM, Carretera Toluca-Atlacomulco Km. 14.5, Toluca 50200, Estado de México, Mexico; nmartinezr@uaemex.mx (N.M.-R.); ed\_ya69@hotmail.com (E.Y.N.-T.); marvals\_18@hotmail.com (M.V.-S.); magciae@uaemex.mx (M.A.G.-E.); mvbasavanagu@uaemex.mx (M.V.B.U.); cbd0044@yahoo.com (C.E.B.-D.)

<sup>2</sup> Facultad de Química, Universidad Autónoma del Estado de México, Paseo Colón esq. Paseo Tollocan, Toluca 50120, Mexico

\* Correspondence: ecuevasy@uaemex.mx; Tel.: +52-722-276-6610 (ext. 7734)

<sup>†</sup> Presented at the 26th International Electronic Conference on Synthetic Organic Chemistry; Available online: <https://ecsoc-26.sciforum.net>.

**Abstract:** Spent, wasted hydroprocessing catalysts from a petrochemical refinery were recovered from a consecutive draining-solvent extraction–calcination strategy. The activity of these recovered heterogeneous catalysts was evaluated in the acid-mediated indole acylation process. Thus, Bis-(indol-3-yl)-alkane diones were obtained when indole was reacted with cyclic anhydrides in presence of DMF as solvent and catalytic amounts of a spent hydroprocessing catalyst waste. In contrast, reaction between indole and phthalic anhydride afforded phthalimide as major product.

**Keywords:** indole; acylation; reuse; spent catalyst

**Citation:** Martínez-Romero, N.; Nolasco-Terrón, E.Y.; Valle-Sánchez, M.; García-Eleno, M.A.; Unnamatla, B.; Barrera-Díaz, C.E.; Cuevas-Yañez, E. Reuse of a Recovered, Spent Hydroprocessing Catalyst in Indole Acylations Using Cyclic Anhydrides. *Chem. Proc.* **2022**, *4*, x. <https://doi.org/10.3390/xxxxx>

Published: 15 November 2022

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## 1. Introduction

Petroleum refining industries use catalysts extensively in many processes with continuous activity causing deposition of contaminants on catalyst surfaces (sometimes carbon and sulfur) which origins gradual deactivation of the catalysts [1]. Hence, the use of heterogeneous catalysts is beneficial for the production of new petrochemical products; however, once the catalysts have been used, final disposal becomes an important issue that represents environmental challenges due to most of these catalysts are made with heavy metals.

In particular, hydroprocessing catalysts combine metals from group VI (Mo, W) with metals from group VIII (Co, Ni) [2], which become a major part of solid wastes after use when these spent catalysts are discarded from hydroprocessing units [3]. Therefore, because of their toxic nature, spent hydroprocessing catalysts are considered as hazardous wastes [4]. Currently, some strategies for environmental impact minimization of spent catalyst waste involve metal leaching [5,6], as well as usage of spent hydrotreating catalysts in other processes, development of improved hydrotreating catalysts, regeneration and reuse and preparation of useful materials from spent catalysts [3].

Recently, our group reported a hydroprocessing spent catalyst recovery method that consisted of a sequential draining-solvent extraction–calcination process affording sulfur-free recovered catalysts which were used in benzyl alcohol oxidations, opening opportunities for wide applications in other organic reactions [7].

This background prompted us to propose the use of recovered, spent hydroprocessing catalysts for the electrophilic acylation of indole, an important process for the preparation of several indole-based natural products and diverse compounds of pharmaceutical interest [8]. In this report we disclose our most recent findings in this area.

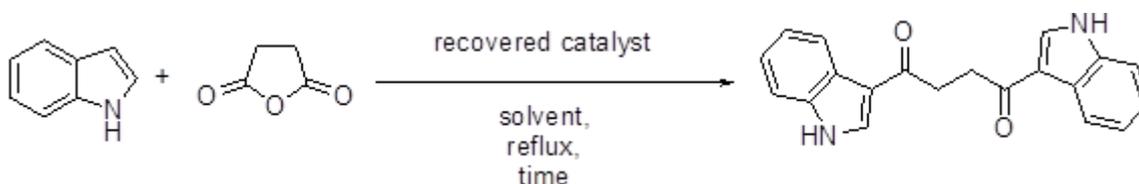
## 2. Results and Discussion

Preliminary experiments were conducted in order to recover spent catalyst waste. According to Cortés-Torres and coworkers [7], direct draining of spent catalysts allowed removal of most of oil and other impurities derived from hydroprocessing process. Drained catalysts underwent a solvent extraction and subsequent calcination, affording treated, recovered catalysts, whose chemical analysis agrees with referred report. A general view of catalysts before and after this treatment is provided in Figure 1.



**Figure 1.** A general view of catalysts before (a) and after (b) draining-solvent extraction-calcination treatment.

Recovered catalysts were tested in acylation of indole with succinic anhydride according to Scheme 1 using diverse solvents under different catalyst ratios and reaction times. The results, summarized in Table 1, show that 1,4-bis-(indol-3-yl)-butane-1,4-dione was obtained in all cases in 5–28% yields.

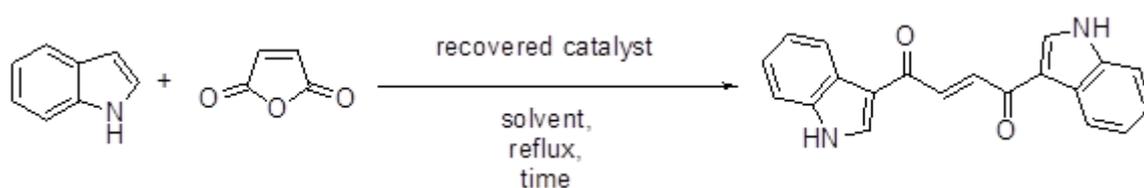


**Scheme 1.** Acylation of indole with succinic anhydride.

**Table 1.** Acylation of indole with succinic anhydride.

Entry	Catalyst Ratio (mg Catalyst/mmol Indole)	Solvent	Reaction Time (h)	%Yield
1	10	THF	24	5
2	10	CDCl <sub>3</sub>	24	5
3	10	AcOEt	24	5
4	10	toluene	24	7
5	5	xylene	24	10
6	10	xylene	48	12
7	5	DMF	24	10
8	10	DMF	24	15
9	10	DMF	48	22
10	10	DMF	72	28

A similar behavior was noted when indole reacted with maleic anhydride in presence of recovered catalysts affording the respective 1,4-bis-(indol-3-yl)-but-2-ene-1,4-dione in 5–15% yields (Scheme 2, Table 2).



**Scheme 2.** Acylation of indole with maleic anhydride.

**Table 2.** Acylation of indole with maleic anhydride.

Entry	Catalyst Ratio (mg Catalyst/mmol Indole)	Solvent	Reaction Time (h)	%Yield
1	10	AcOEt	24	5
2	10	toluene	24	6
3	5	xylene	24	10
4	10	xylene	48	12
5	10	DMF	24	11
6	10	DMF	48	12
7	10	DMF	72	15

An outstanding finding is the formation of N-methyl phthalimide from reaction of indole and phthalic anhydride at 150 °C represented in Scheme 3. Yields up to 62% were obtained using DMF as solvent for 96 h as seen in Table 3. This unexpected result is probably due to acylation of methylamine derived from DMF fragmentation promoted by high temperatures [9–11]. This fact has triggered investigations about this process, and we are currently performing further experiments in order to elucidate the mechanistic details which could help to predict the course of these reactions.



**Scheme 3.** Acylation of indole with phthalic anhydride.

**Table 3.** Acylation of indole with phthalic anhydride.

Entry	Catalyst Ratio (mg Catalyst/mmol Indole)	Solvent	Reaction Time (h)	%Yield
1	10	AcOEt	24	0
2	10	toluene	24	0
3	10	xylene	24	0
4	10	xylene/DMF	48	5
5	10	DMF	48	32
6	10	DMF	72	52
7	10	DMF	96	62

To the best of our knowledge, these are the first examples about the use of spent, wasted hydroprocessing catalysts in indole electrophilic substitutions, which represents an alternative catalytic system for this kind of chemical transformations. The formation of N-methyl phthalimide from indole and phthalic anhydride as exclusive product represents a synthetic challenge that will be studied in future, opening a new trend in this area.

### 3. Experimental

The starting materials were purchased from Aldrich Chemical Co. and were used without further purification. The solvents were distilled before use. Silica plates of 0.20 mm thickness were used for thin layer chromatography. Melting points were determined with a Krüss Optronic melting point apparatus, and they were uncorrected.  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were recorded using a Bruker Avance 300-MHz; the chemical shifts ( $\delta$ ) are given in ppm relative to TMS as an internal standard (0.00). For analytical purposes, the mass spectra were recorded on a Shimadzu GCMS-QP2010 Plus in the EI mode, 70 eV, and 200 °C via direct inlet probe. Only the molecular and parent ions ( $m/z$ ) are reported. IR spectra were recorded on a Bruker Tensor 27.

#### 3.1. General Procedure for Catalyst Recovery

According to a previous report described by our group [7], spent catalyst waste was added to the appropriate solvent and the resulting mixture was stirred and refluxed at indicated conditions. The mixture was cooled to room temperature and the catalyst was filtered and washed. Treatment by calcination afforded recovered catalysts which were used without further purification. Subsequent characterization data correspond to the literature [7].

#### 3.2. General Procedure for Indole Acylations

Recovered catalyst pellets (0.010 g) were added to a solution of the respective cyclic anhydride (1.1 mmol) and indole (0.117 g, 1 mmol) in the appropriate solvent (10 mL). The resulting mixture was heated at reflux temperature for 24 h. The mixture was cooled to room temperature and filtered and the solvent was removed under reduced pressure. The final product was purified by column chromatography ( $\text{SiO}_2$ , hexane/AcOEt 8:2).

##### 3.1.1.1,4-bis-(indol-3-yl)-butane-1,4-dione

Indole and succinic anhydride afforded 1,4-bis-(indol-3-yl)-butane-1,4-dione as a white solid (28%). IR (ATR)  $\nu_{\text{max}}$  3880, 2930, 2850, 1710  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.85 (s, 2H), 7.63 (m, 2H), 7.20 (m, 2H), 7.11 (m, 2H), 6.92 (m, 1H), 4.25 (s, 4H).  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  194.5, 136.9, 127.5, 122.2, 121.9, 119.2, 119.1, 115.7, 111.1, 30.0.

##### 3.1.2.1,4-bis-(indol-3-yl)-but-2-ene-1,4-dione

Indole and maleic anhydride 1,4-bis-(indol-3-yl)-but-2-ene-1,4-dione (15%). IR (ATR)  $\nu_{\text{max}}$  3420, 1690, 1590  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.87 (m, 2H), 7.63 (m, 2H), 7.35 (s, 2H), 7.21 (m, 2H), 7.11 (m, 2H), 6.92 (m, 2H).  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  172.9, 136.5, 135.1, 127.6, 122.2, 121.9, 119.3, 119.1, 115.8, 111.1.

##### 3.1.3. N-methyl phthalimide

Indole and phthalic anhydride afforded N-methyl phthalimide as a white solid (62%). IR (ATR)  $\nu_{\text{max}}$  1760, 1721  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.83 (s, 2H), 7.69 (s, 2H), 24.15 (s, 3H).  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  168.8, 133.9, 132.4, 123.5, 24.4; MS [EI+]  $m/z$  (%): 161 [M]<sup>+</sup> (95), 132 [M- NCH<sub>3</sub>]<sup>+</sup> (35), 104 [M- CONCH<sub>3</sub>]<sup>+</sup> (90), 76 [C<sub>6</sub>H<sub>4</sub>]<sup>+</sup> (100).

### 4. Conclusions

Recovered spent, wasted hydroprocessing catalysts represent a promising source of heterogeneous catalysts for indole electrophilic substitutions in mild conditions that does not requires other additives, expanding the possibilities to carry out reactivity studies with other electrophiles. The simplicity of this synthetic protocol suggests a widespread application.

**Author Contributions:** Conceptualization, C.E.B.-D. and E.C.-Y.; methodology, N.M.-R., E.Y.N.-T. and M.V.-S.; formal analysis, M.A.G.-E., M.V.B.U. and E.C.-Y.; investigation, N.M.-R. and M.V.-S.; resources, M.V.B.U. and E.C.-Y.; data curation, M.A.G.-E., and M.V.B.U.; writing—original draft preparation, C.E.B.-D. and E.C.-Y.; writing—review and editing, E.C.-Y.; visualization, E.C.-Y.; supervision, E.C.-Y.; project administration, C.E.B.-D. and E.C.-Y.; funding acquisition, C.E.B.-D. and E.C.-Y. All authors have read and agreed to the published version of the manuscript.

**Funding:** This research was funded by CONACYT-Mexico, project No. A1-S-18230.

**Institutional Review Board Statement:** Not applicable.

**Informed Consent Statement:** Not applicable.

**Data Availability Statement:** Not applicable.

**Acknowledgments:** Financial support from CONACYT is gratefully acknowledged. The authors would like to thank Armando Ramirez-Serrano for catalyst waste donation management, and to N. Zavala, A. Nuñez, L. Triana, and M. C. Martínez for the technical support.

**Conflicts of Interest:** The authors declare no conflicts of interest.

## References

1. Rogoff, M.J.; Screve, F. *Waste-to-Energy, Second Edition: Technologies and Project Implementation*, 2nd ed.; Elsevier: Oxford, UK, 2011.
2. Marcilly, C. Present status and future trends in catalysis for refining and petrochemicals. *J. Catal.* **2003**, *216*, 47–62.
3. Marafi, M.; Stanislaus, A. Spent catalyst waste management: A review-Part I—Developments in hydroprocessing catalyst waste reduction and use. *Resour. Conserv. Recy.* **2008**, *52*, 859–873.
4. Marafi, M.; Stanislaus, A. Options and processes for spent catalyst handling and utilization. *J. Hazard. Mater.* **2003**, *B101*, 123–132.
5. Al-Sheeha, H.; Marafi, M.; Raghavan, V.; Rana, M.S. Recycling and Recovery Routes for Spent Hydroprocessing Catalyst Waste. *Ind. Eng. Chem. Res.* **2013**, *52*, 12794–12801.
6. Alonso, F.; Ramírez, S.; Ancheyta, J.; Mavil, M. Alternatives for recovering of metals from heavy hydrocarbons spent hydrotreating catalysts: A case of study. *Rev. Int. Contam. Ambient.* **2008**, *24*, 55–69.
7. Cortés-Torres, R.; Nolasco-Terrón, E.Y.; Olea-Mejia, O.; Varela-Guerrero, V.; Barrera-Díaz, C.E.; Cuevas-Yañez, E. Solvent mediated impurity removal process for a spent hydroprocessing catalyst and its use in alcohol oxidations. *Catal. Today* **2018**, *305*, 126–132.
8. Sundberg, R.J. Electrophilic Substitution Reactions of Indoles. In *Heterocyclic Scaffolds II: Reactions and Applications of Indoles*; Gribble, G.W., Ed.; Springer: Heidelberg, Germany, 2010; pp. 47–116.
9. Diao, X.; Yang, D.; Yang, Q.; Cai, X. N,N-Dimethylformamide: An Versatile Organic Synthetic Reagent. *Chin. J. Org. Chem.* **2021**, *41*, 1434–1446.
10. Bras, J.; Muzart, J. Recent Uses of N,N-Dimethylformamide and N,N-Dimethylacetamide as Reagents. *Molecules* **2018**, *23*, 1939.
11. Heravi, M.M.; Ghavidel, M.; Mohammadkhani, L. Beyond a solvent: Triple roles of dimethylformamide in organic chemistry. *RSC Adv.* **2018**, *8*, 27832–27862.